REMARKS

Claims 70-93 are pending. Claim 70 and its dependents have been revised to refer to an "oligodeoxyribonucleotide". No new matter has been added.

Restriction/Election

The Applicants previously elected with traverse **Group I**, claims 18-24, drawn to an ISO comprising an octameric CG motif (i.e., AACGTTAT). No election of species requirement was imposed along with the Restriction Requirement. Dependent claim 77 as directed to SEQ ID NOS: 18, 19 and 47 has been withdrawn from consideration as being directed to a non-elected invention. However, since this is a dependent claim, it clearly falls within previously elected Group I.

Should this requirement be maintained the Applicants reserve the right to file a divisional application and avoid obviousness double patenting rejection of a claim directed to the species of SEQ ID NOS: 18, 19 and 47 which presently fall within generic claim 70.

Rejection—35 U.S.C. §102(b)

Claims 70-73 were rejected under 35 U.S.C. 102(b) as being anticipated by Clark, et al., BI881470. This rejection may be withdrawn, since Clark et al. do not disclose a 20 to 100 deoxynucleotide containing a nonmethylated octameric CG motif of the sequence AACGTTAT. Clark et al. disclose a 97 base oligoribonucleotide (mRNA) containing the octameric CG motif of the sequence AACGTTAT, and cDNA clone IMAGE 4468146 derived from the pT7T3D vector. This cDNA clone consists of a nearly 3000 bp deoxynucleotide sequence (the empty vector is 2897 bp) containing the octameric CG motif of the sequence AACGTTAT and does not consist of 20-100 oligodeoxyribonucleotides. Accordingly, this rejection should now be withdrawn.

Rejection—35 U.S.C. §103(a)

Claims 70-76, 78-83 and 89-92 were rejected under 35 U.S.C. §103(a) as being unpatentable over Schwartz, et al., U.S. Patent No. 6,562,796. Schwartz does not render the invention obvious, because it does not suggest the motif AACGTTAT required by independent claim 70 nor provide a reasonable expectation of success that deoxyribonucleotides containing this motif would have antitumoral activity. As explained below, the choice of the two additional bases adjacent to the 3' of the 5'- purine-purine-CG-pyrimidine-pyrimidine -3' is important for obtaining anti-tumor activity and is not a trivial choice.

While the specification indicates that many oligonucleotides comprising a 5 '-purine-purine-CG-pyrimidine-pyrimidine -3' sequence are known to have immunostimulatory properties, the antitumor activity of only a few sequences, among those described has been effectively demonstrated and the exact nature of the active sequences for producing antitumor activity is not clearly defined.

The invention solves these problems and provides oligonucleotides comprising an immunomodulatory sequence 5'-purine-purine-CG-pyrimidine-pyrimidine -3' (immunomodulatory oligonucleotides or ISS) which have superior antitumor activity. These problems are solved by selecting oligodeoxynucleotides comprising at least one nonmethylated octameric CG motif of the sequence AACGTTAT which have increased antitumor activity compared to other octameric CG motif, including the sequences AACGTTATCC, AACGTTATCG disclosed in Schwartz et al.

The specification shows that oligonucleotides having the octameric motif AACGTTAT (such as An 15 or SEQ ID NO: 9: example 13 and figure 10, example 12 and

figure 7; An21 or SEQ ID NO: 10: example 13 and figure 9) have enhanced activity compared to other nucleotides not having this motif (such as An14, SEQ ID NO: 3: figure 10). Furthermore, the specification provides a detailed analysis of the effect of the sequence of the octameric motif on the antitumor activity (example 13: figures 8 to 10 and 11); not less than 12 oligonucleotides having a different octameric motif were compared. The results presented in figures 8 to 10 and 11 clearly show that the octameric motif AACGTTAT has enhanced activity compared to other motifs not having AT adjacent to AACGTT (An23 (AC), An24(AG), An26(GT), An28(CC), PT1(CG); figure 11). Therefore, the choice of the two additional bases adjacent to the 3' of the 5'- purine-purine-CG-pyrimidine-pyrimidine -3' is not trivial for providing the antitumoral activity of the immunomodulatory oligonucleotides and there is no suggestion or reasonable expectation of success for selecting the motif of the invention.

Schwartz et al. disclose modified ISS comprising the sequence 5'-purine-purine-mC-G-pyrimidine-pyrimidine -3' wherein mC is a modified cytosine and modified ISS selected from: AAmCGTTATCC, AAmCGTTATCG, GAmCGTTCC or GAmCGTTCG. However, Schwartz et al. is totally silent about any effect of the CC or CG adjacent to the 5' end of the 5'-purine-purine-mC-G-pyrimidine-pyrimidine -3' sequence. Schwartz et al. teach only that the immunomodulatory oligonucleotides comprising an ISS with a modified cytosine are more effective to stimulate IL-6, 1L-12 production or lymphocyte proliferation *in vitro*, than the oligonucleotides comprising an ISS with an unmodified cytosine. Furthermore, Schwartz et al. neither demonstrate any therapeutic effect, nor any antitumoral effect of the immunomodulatory oligonucleotides comprising a modified cytosine nor cannot provide a reasonable expectation of success for the superior functional properties of the invention.

Therefore, the oligodeoxynucleotide comprising at least one nonmethylated octameric CG motif of the sequence AACGTTAT is not obvious over Schwartz et al. which disclose

immunostimulatory oligonucleotides of a different immunomodulatory sequence with a modified cytosine and without any antitumor activity. Accordingly, the Applicants respectfully request that this rejection be withdrawn.

Rejection—Double Patenting

Claims 84-88 and 93 were rejected under the judicially-created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 3, 4 and 6-9 of U.S. Patent No. 7,108,844. The Applicants respectfully traverse this rejection in view of the differences in scope between the prior patented claims and the presently rejected claims. Other than assert that the claims comprise SEQ ID NO: 51, the Office has not explained why the rejected claims would be patentably indistinct from the claims of the '844 patent, especially in view of the rationale applied in the Restriction Requirement of record.

In the event that this ground of rejection is maintained, the Applicants respectfully request that this rejection be held in abeyance pending the identification of otherwise allowable subject matter. At that time, if necessary, a terminal disclaimer may be filed.

Allowable Subject Matter

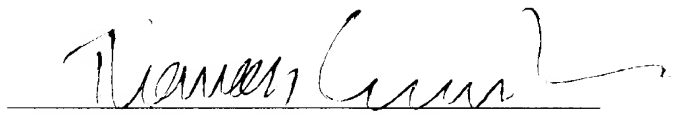
The Applicants thank Examiner Zara for indicating that the subject matter of Claim 77 as drawn to SEQ ID NOS: 9, 10, 16, 21, 31, and 33-35 is free of the prior art. The Applicants respectfully request that the objection to claim 77 be withdrawn as SEQ ID NOS: 18, 19 and 47 fall within the scope of generic claim 70.

Conclusion

This application presents allowable subject matter and the Examiner is respectfully requested to pass it to issue. The Examiner is kindly invited to contact the undersigned should a further discussion of the issues or claims be helpful.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.
Norman F. Oblon



Thomas M. Cunningham, Ph.D.
Registration No. 45,394

Customer Number
22850

Tel: (703) 413-3000
Fax: (703) 413 -2220
(OSMMN 08/07)